CLAIMS

1. Polyepitopic fragments of the E6 or E7 protein of HPV, characterized in that they comprise a peptide sequence of about 15 to 30 amino acids, this peptide sequence containing amino acid sequences of at least 3 different epitopes binding stably to HLA molecules of identical or different type, when these epitopes are obtained by enzymatic degradation of said peptide sequence, particularly in the proteasome, such that at least 4 HLA molecules of different types bind to these epitopes, these 4 HLA molecules being selected from among those of types A1, A2, A3, A11, A24, A29, B7, B8, B18, B27, B35, B44, B51 and B62.

2. Polyepitopic fragments according to claim 1, characterized in that the number of amino acids of their peptide sequence is greater than or equal to 17, and less than or equal to 30.

3. Polyepitopic fragments of the E6 protein of HPV according to claim 1 or 2, characterized in that they comprise a peptide sequence of about 15 to 30 amino acids, this peptide sequence containing amino acid sequences of at least 5 different epitopes binding stably to HLA molecules of identical or different type, when these epitopes are obtained by enzymatic degradation of said peptide sequence, particularly in the proteasome, such that at least 6 HLA molecules of different types bind to these epitopes, these 6 HLA molecules being selected from those of types A1, A2, A3, A11, A24, A29, B7, B8, B18, B27, B35, B44 and B51.

4. Polyepitopic fragments of the E6 protein of HPV according to one of claims 1 to 3, characterized in that they all comprise an epitope binding to the HLA molecule of type B35, an epitope binding to the HLA molecule of type B44, and an epitope binding to the HLA molecule of type B51.

5. Polyepitopic fragment of the E6 protein of HPV according to one of claims 1 to 4, characterized in that it corresponds to the fragment of 30 amino acids delimited by the

amino acids located in positions 15 and 44 of the peptide sequence of the E6 protein of HPV, and characterized by the peptide sequence SEQ ID NO: 4 as follows:

(15)RPRKLPQLCTELQTTIHDIILECVYCKQQL(44)

said fragment containing 9 epitopes binding stably to at least one of the 8 HLA molecules of the following types: A2, A11, A29, B7, B8, B35, B44, or B51, said epitopes being the following:

-(15)RPRKLPQL(22) binding stably to HLA molecules of the B7 or B35 type,

-(18)KLPQLCTEL(26) binding stably to HLA molecules of the A2 type,

-(19)LPQLCTEL(26) binding stably to HLA molecules of the B51 type,

-(21)QLCTELQTTI(30) binding stably to HLA molecules of the A2 type,

-(24)TELQTTIHDI(33) binding stably to HLA molecules of the A29 or B44 type,

-(29)TIHDIILRCV(38) binding stably to HLA molecules of the A2 type,

-(33)IILECVYCK(41) binding stably to HLA molecules of the A11 type,

-(35)LECVYCKQQL(44) binding stably to HLA molecules of the A29 or B44 type,

-(37)CVYCKQQL(44) binding stably to HLA molecules of the B8 type.

6. Polyepitopic fragment of the E6 protein of HPV according to one of claims 1 to 4, characterized in that it corresponds to the fragment of 17 amino acids delimited by the amino acids located in positions 46 and 62, or to the fragment of 22 amino acids delimited by the amino acids located in positions 46 and 67 of the peptide sequence of the E6 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 6 as follows:

(46)RREVYDFAFRDLCIVYRDGNPY(67)

said fragment containing 6 epitopes binding stably to at least one of the 10 HLA molecules of the following types: A2, A3, A11, A24, A29, B7, B27, B35, B44, or B51, said epitopes being the following:

-(46)RREVYDFAFR(55) binding stably to HLA molecules of the B27 type,

-(49)VYDFAFRDL(57) binding stably to HLA molecules of the A24 type,

-(50)YDFAFRDL(57) binding stably to HLA molecules of the A29 or B44 type,

-(52)FAFRDLCIV(60) binding stably to HLA molecules of the A2, B35, B51, or B7 type,

-(54)FRDLCIVYR(62) binding stably to HLA molecules of the A3 or A11 type,

-(59)IVYRDGNPY(67) binding stably to HLA molecules of the A3 or A11 type.

7. Polyepitopic fragment of the E6 protein of HPV according to one of claims 1 to 4, characterized in that it corresponds to the fragment of 29 amino acids delimited by the amino acids located in positions 80 and 108 of the peptide sequence of the E6 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 8 as follows:

(80)ISEYRHYCYSLYGTTLEQQYNKPLCDLLI(108)

said fragment containing 6 epitopes binding stably to at least one of the 10 HLA molecules of the following types: A1, A3, A11, A24, A29, B7, B18, B35, B44, or B51, said epitopes being the following:

-(80)ISEYRHYCY(88) binding stably to HLA molecules of the A1 or B18 type,

-(81)SEYRHYCY(88) binding stably to HLA molecules of the A29 or B44 type,

-(87)CYSLYGTTL(95) binding stably to HLA molecules of the A24 type,

-(94)TLEQQYNK(101) binding stably to HLA molecules of the A3 or A11 type,

-(95)LEQQYNKPL(103) binding stably to HLA molecules of the A29 or B44 type,

-(101)KPLCDLLI(108) binding stably to HLA molecules of the B7, B35 or B51 type.

8. Polyepitopic fragment of the E6 protein of HPV according to one of claims 1 to 4, characterized in that it corresponds to the fragment of 22 amino acids delimited by the amino acids located in positions 118 and 139 of the peptide sequence of the E6 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 10 as follows:

(118)CPEEKQRHLDKKQRFHNIRGRW(139)

said fragment containing 6 epitopes binding stably to at least one of the 7 HLA molecules of the following types: A24, B8, B18, B27, B35, B44, or B51, said epitopes being the following:

-(118)CPEEKQRHL(126) binding stably to HLA molecules of the B8, B18, B35, B51 type,

-(119)PEEKQRHL(126) binding stably to HLA molecules of the B44 type,

-(127)DKKQRFHNI(135) binding stably to HLA molecules of the B8 type,

-(128)KKQRFHNIR(136) binding stably to HLA molecules of the B27 type,

-(130)QRFHNIRGRW(139) binding stably to HLA molecules of the B27 type,
-(131)RFHNIRGRW(139) binding stably to HLA molecules of the A24 type.

9. Polyepitopic fragments of the E7 protein of HPV according to claim 1 or 2, characterized in that they comprise a peptide sequence of about 15 to 30 amino acids, this peptide sequence containing amino acid sequences of at least 3 different epitopes binding stably to HLA molecules of identical or different type, when these epitopes are obtained by enzymatic degradation of said peptide sequence, particularly in the proteasome, such that at least 4 HLA molecules of different types bind to these epitopes, these 4 HLA molecules being selected from those of type A1, A2, A3, A11, A29, B7, B18, B35, B44 and B62.

10. Polyepitopic fragments of the E7 protein of HPV according to claim 9, characterized in that they all comprise an epitope binding to the HLA molecule of type B44.

11. Polyepitopic fragment of the E7 protein of HPV according to one of claims 9 or 10, characterized in that it corresponds to the fragment of 23 amino acids delimited by the amino acids located in positions 3 and 25 of the peptide sequence of the E7 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 14 as follows:

(3)GDTPTLHEYMLDLQPETTDLYCY(25)

said fragment containing 5 epitopes binding stably to at least one of the 6 HLA molecules of the following types: A1, A2, B18, B35, B44 or B62, said epitopes being the following:

-(3)GDTPTLHEY(11) binding stably to HLA molecules of the B44 type,
-(5)TPTLHEYML(13) binding stably to HLA molecules of the B35 type,
-(11)YMLDLQPETT(20) binding stably to HLA molecules of the A2 type,
-(15)LQPETTDLY(23) binding stably to HLA molecules of the B62 type,
-(16)QPETTDLYCY(25) binding stably to HLA molecules of the A1 or B18 type.

12. Polyepitopic fragment of the E7 protein of HPV according to one of claims 9 or 10, characterized in that it corresponds to the fragment of 17 amino acids delimited by the

amino acids located in positions 44 and 60 of the peptide sequence of the E7 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 16 as follows:

(44)QAEPDRAHYNIVTFCCK(60)

said fragment containing 4 epitopes binding stably to at least one of the 6 HLA molecules of the following types: A1, A3, A11, A29, B7, B18, B35, or B44, said epitopes being the following:

-(44)QAEPDRAHY(52) binding stably to HLA molecules of the A1 or B18 type,

-(45)AEPDRAHY(52) binding stably to HLA molecules of the A29 or B44 type,

-(46)EPDRAHYNIV(55) binding stably to HLA molecules of the B7 or B35 type,

-(53)NIVTFCCK(60) binding stably to HLA molecules of the A3 or A11 type.

13. Polyepitopic fragment of the E7 protein of HPV according to one of claims 9 or 10, characterized in that it corresponds to the fragment of 19 amino acids delimited by the amino acids located in positions 79 and 97 of the peptide sequence of the E7 protein of HPV, this latter fragment being characterized by the peptide sequence SEQ ID NO: 18 as follows:

(79)LEDLLMGTLGIVCPICSQK(97)

said fragment containing 4 epitopes binding stably to at least one of the 5 HLA molecules of the following types: A2, A3, A11, A29 or B44, said epitopes being the following:

-(79)LEDLLMGTL(87) binding stably to HLA molecules of the A29 or B44 type,

-(82)LLMGTLGIV(90) binding stably to HLA molecules of the A2 type,

-(86)TLGIVCPI(93) binding stably to HLA molecules of the A2 type,

-(89)IVCPICSQK(97) binding stably to HLA molecules of the A3 or A11 type.

14. Polyepitopic fragments of the E6 or E7 protein according to one of claims 1 to 13, characterized in that they correspond to the peptide sequences derived from the polyepitopic fragments defined in one of claims 1 to 13, particularly:

– by substitution, and/or suppression, and/or addition of one or several amino acids, of the above-mentioned fragments, and/or

– by modification of at least one –CO-NH- peptide linkage of the peptide chain of the above-mentioned fragments, particularly by introduction of a retro or retro-inverso type linkage, and/or

– by substitution of at least one amino acid of the peptide chain of the sequence or of the above-mentioned fragment, with a non-proteinogenic amino acid,

said derived sequences containing peptides or pseudopeptides binding specifically to the same molecule or molecules of MCH as those binding to the peptides contained in the above-mentioned polyepitopic fragments from which they derive.

15. Nucleotide sequences coding for a polyepitopic fragment or for a peptide sequence derived according to one of claims 1 to 14, said nucleotide sequences being derived from the sequence SEQ ID NO: 1 coding for the E6 protein, or from the sequence SEQ ID NO: 11 coding for the E7 protein.

16. Nucleotide sequences according to claim 15, selected from the following:

– the sequence SEQ ID NO: 3, coding for the polyepitopic fragment SEQ ID NO: 4 according to claim 5,

– the sequence SEQ ID NO: 5, coding for the polyepitopic fragment SEQ ID NO: 6 according to claim 6,

– the sequence SEQ ID NO: 7, coding for the polyepitopic fragment SEQ ID NO: 8 according to claim 7,

– the sequence SEQ ID NO: 9, coding for the polyepitopic fragment SEQ ID NO: 10 according to claim 8,

– the sequence SEQ ID NO: 13, coding for the polyepitopic fragment SEQ ID NO: 14 according to claim 11,

– the sequence SEQ ID NO: 15, coding for the polyepitopic fragment SEQ ID NO: 16 according to claim 12,

– the sequence SEQ ID NO: 17, coding for the polyepitopic fragment SEQ ID NO: 18 according to claim 13.

17. Polyclonal or monoclonal antibodies, directed against a polyepitopic fragment or against a peptide sequence derived according to one of claims 1 to 14.

18. Lipopeptide characterized in that it comprises:

– a peptide portion comprising one or several polyepitopic protein fragments, or a peptide sequence derived from said fragments, as defined in one of claims 1 to 14,

– and one or several lipophile portions, such as those comprising:

* a C4 to C20 hydrocarbon chain, saturated or unsaturated, linear or branched,

* or a steroid group, as the case may be bonded to the above-mentioned hydrocarbon chain,

said lipophilic portions being if desired associated with a short peptide vector comprising one or several ionized functions at physiological pH, and a function permitting the covalent bonding of said hydrocarbon chain and/or said steroid group.

19. Pharmaceutical composition, or vaccine, characterized in that it comprises:

* a)

– at least one polyepitopic fragment of the E6 or E7 protein defined in one of claims 1 to 13,

– and/or at least one peptide sequence derived from this fragment, as defined in claim 14,

– and/or at least one suitable vector, particularly lipopeptides according to claim 18 and/or micelles, containing at least one above-mentioned polyepitopic fragment of the E6 or E7 protein, and/or at least one above-mentioned sequence derived from these fragments,

in association with a physiologically acceptable vehicle,

said polyepitopic protein fragment and/or its derived sequence being, as the case may be, associated with one or several other exogenous epitopes recognized by auxiliary T cells, such as the peptide fragment delimited by the amino acids located in positions 830 and 846 of the peptide sequence of the tetanus toxin, hemagglutinin, or PADRE epitope,

* or b)

– at least one nucleotide sequence according to claim 15 or 16, coding for an above-mentioned polyepitopic fragment of the E6 or E7 protein,

– and/or at least one nucleotide sequence coding for a peptide sequence derived from this fragment, as defined above,

– and/or at least one above-mentioned suitable vector, selected particularly from the viruses, containing at least one above-mentioned nucleotide sequence,

in association with a physiologically acceptable vehicle,

* or c)

– antibodies according to claim 17, directed against a polyepitopic fragment of the E6 or E7 protein, and/or against a peptide sequence derived from these fragments, as defined above.

20. The use of polyepitopic fragments of the E6 or E7 protein defined in one of claims 1 to 13, or the derived peptide sequences according to claim 14, or the nucleotide sequences according to claims 15 or 16, or of antibodies according to claim 17, or the lipopeptides according to claim 18, for the preparation of a medication or vaccine adapted for the prevention or treatment of pathologies connected with the infection of individuals by human papillomavirus, such as cervical intraepithelial neoplasias (CIN), invasive cancer of the neck of the uterus, vulvar intraepithelial neoplasias (VIN).

21. Epitopes of the E6 protein of HPV selected from the following:
-(19)LPQLCTEL(26) binding stably to HLA molecules of the B51 type,
-(21)QLCTELQTTI(30) binding stably to HLA molecules of the A2 type,
-(24)TELQTTIHDI(33) binding stably to HLA molecules of the A29 or B44 type,
-(33)IILECVYCK(41) binding stably to HLA molecules of the A11 type,
-(35)LECVYCKQQL(44) binding stably to HLA molecules of the A29 or B44 type,
-(37)CVYCKQQL(44) binding stably to HLA molecules of the B8 type,
-(46)RREVYDFAFR(55) binding stably to HLA molecules of the B27 type,
-(49)VYDFAFRDL(57) binding stably to HLA molecules of the A24 type,
-(50)YDFAFRDL(57) binding stably to HLA molecules of the A29 or B44 type,
-(52)FAFRDLCIV(60) binding stably to HLA molecules of the A2, B35, B51, or B7 type,
-(54)FRDLCIVYR(62) binding stably to HLA molecules of the A3 or A11 type,
-(59)IVYRDGNPY(67) binding stably to HLA molecules of the A3 or A11 type,

-(81)SEYRHYCY(88) binding stably to HLA molecules of the A29 or B44 type,
-(87)CYSLYGTTL(95) binding stably to HLA molecules of the A24 type,
-(94)TLEQQYNK(101) binding stably to HLA molecules of the A3 or A11 type,
-(95)LEQQYNKPL(103) binding stably to HLA molecules of the A29 or B44 type,
-(101)KPLCDLLI(108) binding stably to HLA molecules of the B7, B35 or B51 type,
-(118)CPEEKQRHL(126) binding stably to HLA molecules of the B8, B18, B35, B51 type,
-(119)PEEKQRHL(126) binding stably to HLA molecules of the B44 type,
-(127)DKKQRFHNI(135) binding stably to HLA molecules of the B8 type,
-(128)KKQRFHNIR(136) binding stably to HLA molecules of the B27 type,
-(130)QRFHNIRGRW(139) binding stably to HLA molecules of the B27 type,
-(131)RFHNIRGRW(139) binding stably to HLA molecules of the A24 type.

22. Epitopes of the E7 protein of HPV selected from the following:
-(3)GDTPTLHEY(11) binding stably to HLA molecules of the B44 type,
-(5)TPTLHEYML(13) binding stably to HLA molecules of the B35 type,
-(15)LQPETTDLY(23) binding stably to HLA molecules of the B62 type,
-(16)QPETTDLYCY(25) binding stably to HLA molecules of the A1 or B18 type,
-(45)AEPDRAHY(52) binding stably to HLA molecules of the A29, B44 type,
-(46)EPDRAHYNIV(55) binding stably to HLA molecules of the B7 or B35 type,
-(53)NIVTFCCK(60) binding stably to HLA molecules of the A3, A11 type,
-(79)LEDLLMGTL(87) binding stably to HLA molecules of the A29, B44 type,
-(89)IVCPICSQK(97) binding stably to HLA molecules of the A3, A11 type.